THE ROLE OF MODELLING AND SIMULATION IN CLINICAL PHARMACOLOGY

L. Aarons*
The University of Manchester, Manchester, United Kingdom

Summary: Pharmacokinetics is a field that has matured over the last 40 years, and we now have a detailed pharmacologic and physiological understanding of "what the body does to a drug." The subject has reached a point whereby reasonably accurate prediction of human pharmacokinetic behavior of a chemical, based on its physicochemical properties and some in vitro experimentation, is possible. Pharmacodynamics as a discipline is even older than pharmacokinetics, but we are not in such a strong position in terms of prediction of human pharmacodynamics, as we are with pharmacokinetics. However, pharmacokinetic/pharmacodynamic (PKPD) modeling is making rapid strides. PKPD is very much a quantitative discipline in the sense that theory can be translated into temporal profiles of concentration or response, even to the extent of being able to design dosage regimens for individual patients. The hub of this quantitative discipline is a PKPD model, and PKPD modeling has become an essential activity in preclinical and clinical drug development and clinical drug usage.

Recently, the European Medicines Agency (EMA) and the European Association of Pharmaceutical Industries and Associates (EFPIA) brought together key opinion leaders and regulatory and academia experts from Europe and beyond to discuss the role of modeling and simulation (M&S) in areas such as early medicine development, clinical pharmacology and dose-finding studies, special populations, optimization, and analysis of pivotal clinical trials.[1] The fact that this meeting occurred indicates there is a meeting of minds on the role of modeling in drug development in particular, across a range of stakeholders. Perhaps modeling is coming in from the cold and is now being seen as part of the solution rather than as part of the problem.

Disclosure of Interest: None declared.

Reference

1. Manolis E, Rohou S, Hemmings R, Salmonson T, Karlsson M, Milligan PA "The Role of Modeling and Simulation in Development and Registration of Medicinal Products: Output From the EFPIA/EMA Modeling and Simulation Workshop." *CPT: Pharmacometrics & Systems Pharmacology*. 2013;2:e31; doi:10.1038/psp.2013.7.

NON INFECTIOUS INTERMEDIATE AND POSTERIOR UVEITIS: TREATMENT AND PLACE OF LOCAL STEROIDS

M. Accorinti*
Dipartimento Organi di Senso, Sapienza Università di Roma, Rome, Italy

Summary: Corticosteroids are considered to be the mainstay of therapy in noninfectious uveitis, until now, but side effects and complications related to such therapy, if systemically given, are well known. This is why in the recent period many local therapies have been proposed to treat noninfectious uveitis, especially intermediate and posterior. Corticosteroids can be given periocularly and intravitreally. Sub-Tenon injection (either via the orbital floor or transconjunctivally in the supero-temporal quadrant) with long-lasting steroids can be used every 15 to 60 days, and it is able to control uveitis as well as to treat macular edema. Apart from typical ocular side effects related to steroid therapy, such as cataract and intraocular pressure (IOP) increase, this way of administration can induce conjunctival and orbital floor fibrotic reaction, ptosis, retrobulbar hemorrhages, muscles paresis, optic nerve injury, and globe perforation. Intravitreal administration of steroids can be done either with a direct injection of triamcinolone, or with the placement into the vitreous cavity of a biodegradable dexamethasone implant (700 μg, 4–6 months' duration) or of a device able to deliver continuously for almost 3 years fluocinolone acetonide (0.59 mg). Their efficacy has been widely proven in treating noninfectious uveitis, but some local side effects (dexamethasone biodegradable implant: IOP increase in 25% of the patients; fluocinolone implant: cataract in 93% of the cases, IOP increase in 77%, 37% of whom requiring a surgical approach) could limit their use. In neither of the 2 aforementioned approaches is there a significant risk of developing endophthalmitis or retinal detachment. A questionable use of local therapy is in patients with an associated systemic disease and/or in those with bilateral uveitis. Nevertheless, in such a case, it is not rare to observe a very severe inflammatory ocular involvement with few systemic symptoms, and/or an asymmetric presentation of uveitis, which can be usefully comanaged with local, either periocular or intravitreal therapy.

Disclosure of Interest: None declared.

TOWARDS BEST REPORTING PRACTICES FOR CLINICAL PHARMACOLOGY TRIALS

D. Altman*
Centre for Statistics in Medicine, University of Oxford, Oxford, United Kingdom

Summary: Abundant evidence from reviews of published research articles has demonstrated that a substantial proportion lack key information. A fundamental principle is that readers need to know exactly what was done and be given an accurate, complete and transparent account of what was found. Readers should not be expected to take on trust that the authors have done a study without flaws. Furthermore, in principle, there should be enough detail to allow replication.

Widespread deficiencies in research publications weaken the evidence base for clinical practice. How can it be that none of the authors, peer reviews, or editors has detected that so many articles are substandard and, indeed, often unfit for purpose? Ensuring that journal articles are of maximum value to readers should be a priority for those who write research articles and those who review them. In recent years, many reporting guidelines have been developed, outlining the key elements of research that should be reported, with as-yet modest success. These and other related resources are available on the Web site of the EQUATOR Ne2rk. The best-known reporting guideline is the CONSORT Statement for reporting randomized trials. Several extensions of CONSORT have been published. In this context, I will discuss the reporting of early clinical studies in pharmacology.

Disclosure of Interest: None declared.

NEW STRATEGIES IN THE TREATMENT OF MAJOR DEPRESSION

F. Artigas*
IIBB(CSIC)-IDIBAPS-CIBERSAM, Barcelona, Spain

Summary: Major depression is a severe psychiatric syndrome with very high prevalence and socioeconomic impact. Its pathophysiology is poorly known, yet several neurotransmitter systems and brain areas have been implicated. Selective serotonin (5-hydroxytryptamine [5(-HT)]) reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs) are the most used antidepressant treat-